The sequencing of lanreotide (LAN) after octreotide LAR (OCT) for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs)


Tulane University School of Medicine, Bostom, MA, USA. *FTI Health Solutions, Research Triangle Park, NC, USA. **Ipsen Biopharmaceuticals, Boxborough, MA, USA. *FTI Health Solutions, Waltham, MA, USA. *Tulane Medical Center, New Orleans, Cancer Center, New Orleans, LA, USA. *Tulane College, New Orleans, LA, USA. *University of New Mexico Health Science, Albuquerque, NM, USA.

BACKGROUND
- Neurouendocrine tumors (NETs), a relatively rare group of neoplasms, are slow growing. Due to the paucity of symptoms in early stages, patients are often diagnosed at an advanced stage or metastatic stage.
- The somatostatin analog (SSA) octreotide and lanreotide depot (lanreotide) are recommended as primary system therapies for patients with advanced or metastatic disease. However, their individual limitations are significant.
- With differences in indication, administration, and the relatively recent approval of lanreotide (December 2015), the United States Food and Drug Administration, clinicians and patients may consider sequencing SSA therapy from long-acting octreotide to lanreotide. However, evidence of the feasibility of sequencing long-acting octreotide to lanreotide treated patients to lanreotide and the resulting effectiveness and safety in real-world settings is limited.

OBJECTIVE
- To evaluate clinical outcomes among patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs) who transitioned from long-acting octreotide monotherapy to lanreotide monotherapy.

METHODS
Study design and patient population:
- We conducted a multicenter, non-interventional, retrospective medical record review of 48 patients who had a confirmed diagnosis of locally advanced or metastatic GEP-NET across six US-based sites.
- Patients aged ≥ 18 years who were of long-acting octreotide monotherapy with lanreotide monotherapy were included. Patients were initiated on SSA therapy with or without other therapies (e.g., tumor shrinkage; chemotherapy; SSA-NET, or had a familial NET syndrome).
- Study measures and analyses:
  - Patient demographics and baseline clinical characteristics were collected.
  - Treatment and outcome measures were observed during the periods of treatment with long-acting octreotide and lanreotide.
  - Patients with disease progression or clinically significant disease were included and followed for a minimum of 6 months, regardless of disease status at the time of transition from SSA to SSA-NET (the time of disease). Individuals in disease were included, and patients were followed for a minimum of 6 months, regardless of disease status at the time of transition from SSA to SSA-NET (the time of disease).

RESULTS
- Treatment with long-acting octreotide and results for transition:
  - At the initial SSA-NET diagnosis, patients began treatment with long-acting octreotide after a mean (SD) of 76 (234.3) months and long-acting octreotide for a mean (SD) of 38.4 (31.8) months.
  - The most common reasons for transition were progressive disease (64/103 [62%]) and patient preference (15/103 [15%]).
- At the time of transition to lanreotide, more than half of patients (56/103 [55%]) had nonprogressive disease, and 60/103 (59%) patients had nonprogressive disease.
- Patients assessed based on imaging, and the remaining had unknown disease status.
- Treatment with lanreotide and tumor assessment:
  - At the end of study follow-up (103/103 [100%]) patients were still receiving lanreotide treatment, and the Kaplan-Meier estimates of progression-free survival (PFS) were 71 (95% CI: 24.7 to 0.6) months.
  - Patients who had the disease progression diagnosis were observed for 22 (79.3%) patients after initiating lanreotide monotherapy (G0 to 50/103 [50%] patients were assessed based on imaging) (Figure 3).
  - The median (95% CI) clinical PFS after treatment with lanreotide was estimated to be 17.7 months (2.9 to 119.2 months).
- Patients who had the disease progression diagnosis were observed for 22 (79.3%) patients after initiating lanreotide monotherapy (G0 to 50/103 [50%] patients were assessed based on imaging) (Figure 3).
- Among patients who had progressive disease at the time of transition to lanreotide, the median (95% CI) clinical PFS was estimated to be 16.5 months (n.a. to 16.5 months).
  - Figures 4 and 5 present the proportion of patients with disease-related symptoms and other AEs during each assessment period.

LIMITATIONS
- Patients included in the study were selected by convenience sample, so study findings may not be generalizable to the overall population of patients with locally advanced or metastatic GEP-NETs.
  - The type and frequency of feeding to assess tumor status in a real-world practice may differ and is a typically more variable than those required in a clinical trial protocol.
  - PFS estimates from the study should be compared with clinical trial estimates with these limitations in mind.
  - Evaluation of progression in this study was not restricted to a validated symptom summary and presented through symptom, biochemical tests, and/or clinical judgement was allowed. However, fewer than 50% of patients were determined to have progressive disease using tumor imaging.
- The requirement for 60 days of lanreotide treatment after transition could have introduced intermediate time bias into survival estimates.

REFERENCES
- The retrospective medical record review assessed the feasibility of sequencing from long-acting octreotide monotherapy to lanreotide monotherapy among patients with locally advanced GEP-NET across multiple sites in the US.
- After receiving long-acting octreotide for an average of 38 months, the median clinical PFS for lanreotide monotherapy was estimated to be 23.7 months (95% CI: 2.9 to 119.2 months).
- Our study suggests that patients with locally advanced or metastatic GEP-NETs previously treated with long-acting octreotide monotherapy can be safely transitioned to lanreotide monotherapy.
- The clinical PFS observed among patients who had either nonprogressive or progressive disease at the time of transition from long-acting octreotide to lanreotide reinforces the possibility of sequencing lanreotide after long-acting octreotide.

Contact Information
Ipsen Biopharmaceuticals, Boxborough, MA, USA
E: daniel.vallotton@ipsen.com
This study was sponsored by Ipsen

The sequencing of lanreotide (LAN) after octreotide LAR (OCT) for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

Wassil M. Saif1, Rohan Parikh2, David Ray3, James A. Kaye4, Samantha K. Kurosky1, Katharine Thomas5, Robert A. Ramirez5, Thorvardur Halfdanarson9, Thomas J.R. Beveridge3, Belayo Mirakhor1, Catherine A. Lubeck6, Saurabh Nagar7, Heliosa Soares2

1Tufts University School of Medicine, Boston, MA, USA; 2RTI Health Solutions, Research Triangle Park, NC, USA; 3Ipsen Biopharmaceuticals, Boxborough, MA, USA; 4RTI Health Solutions, Waltham, MA, USA; 5Oncologic Medical Center-Namur, Neuroendocrine Tumor Program, Namur, LA, USA; 6Mayo Clinic, Rochester, MN, USA; 7University of New Mexico Medical School, Albuquerque, NM, USA.

BACKGROUND

- Neuroendocrine tumors (NETs), a relatively rare group of neoplasms, are slow-growing. Due to a paucity of symptoms in early stages, patients are often diagnosed at an advanced or metastatic stage.1-3
- The somatostatin analogs (SSAs) octreotide and lanreotide depot (lanreotide) are recommended as primary systemic therapy for patients with advanced or metastatic disease4; however, their indications differ.
- With indications in administration, and the relatively recent approval of lanreotide (December 2014) by the United States (US) Food and Drug Administration, clinicians and patients may consider sequencing SSA therapy from long-acting octreotide to lanreotide. However, evidence of the feasibility of sequencing long-acting octreotide-treated patients to lanreotide and the resulting effectiveness and safety in real-world settings is limited.

OBJECTIVE

- To evaluate clinical outcomes among patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs) who transitioned from long-acting octreotide monotherapy to lanreotide monotherapy.

METHODS

- Study design and patient population
  - We conducted a multicenter, noninterventional, retrospective medical record review of 91 patients who had a confirmed diagnosis of locally advanced or metastatic GEP-NET across six US-based sites.
  - Patients aged ≥ 18 years who sequenced long-acting octreotide monotherapy with lanreotide monotherapy were included (minimum 90-day treatment on each drug).
  - Patients were excluded if they had been enrolled in a clinical trial for GEP-NET, had a history of other malignant disease (except basal cell carcinoma or carcinoma in situ of the cervix), were being treated with an SSA in combination with other NET treatments other than immediate release (IR) subcutaneous octreotide, received other primary treatment (e.g., targeted therapy, chemotherapy) for GEP-NET, or had a familial NET syndrome.

RESULTS

- Study design and analyses
  - Patient demographics and baseline clinical characteristics were collected.
  - Treatment and outcome measures were observed during the periods of treatment with long-acting octreotide and lanreotide (Figure 1).
  - Clinician-defined progressive disease was based on local tumor imaging, uncontrolled symptoms, biomarker progression, and/or clinical judgement.
  - Clinical progression-free survival (PFS) was estimated using the Kaplan-Meier method starting at the date of transition to lanreotide.
  - Results were stratified by disease status at the time of transition (i.e., progressive disease, nonprogressive disease, or unknown status).
  - Disease-related symptoms and other adverse events (AEs) were examined for each assessment period (Figure 1).
  - Descriptive analysis was conducted for patient demographics, clinical characteristics, treatment, and outcome measures.

- Table 1 presents patient demographics and clinical characteristics for 91 patients included in the study.

Table 1. Patient demographics and clinical characteristics

<table>
<thead>
<tr>
<th>Total patient sample, (N)</th>
<th>91</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, (n, %)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>54 (59.3%)</td>
</tr>
<tr>
<td>Race, (n, %)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>83 (91.2%)</td>
</tr>
<tr>
<td>Black/African American</td>
<td>5 (5.5%)</td>
</tr>
<tr>
<td>Others/don't know</td>
<td>3 (3.3%)</td>
</tr>
<tr>
<td>Clinical stage at initial diagnosis, (n, %)</td>
<td></td>
</tr>
<tr>
<td>Stage I/II/III</td>
<td>6 (6.6%)</td>
</tr>
<tr>
<td>Stage IV</td>
<td>65 (71.4%)</td>
</tr>
<tr>
<td>Don't know</td>
<td>20 (22.0%)</td>
</tr>
<tr>
<td>Primary tumor site of NET, (n, %)</td>
<td></td>
</tr>
<tr>
<td>Small intestine</td>
<td>58 (63.7%)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>13 (14.3%)</td>
</tr>
<tr>
<td>Colon/appendix</td>
<td>7 (7.7%)</td>
</tr>
<tr>
<td>Other primary tumor site</td>
<td>7 (7.7%)</td>
</tr>
<tr>
<td>Unknown origin/don’t know</td>
<td>6 (6.6%)</td>
</tr>
<tr>
<td>Age at diagnosis of locally advanced or metastatic GEP-NET</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>57 (10.9)</td>
</tr>
<tr>
<td>Common sites of distant metastasis at locally advanced or metastatic GEP-NET, (n, %)</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>65 (71.4%)</td>
</tr>
<tr>
<td>Lymph node(s)</td>
<td>34 (37.4%)</td>
</tr>
<tr>
<td>Peritoneal cavity</td>
<td>8 (8.8%)</td>
</tr>
<tr>
<td>Functional status at locally advanced or metastatic GEP-NET, (n, %)</td>
<td></td>
</tr>
<tr>
<td>Functional disease</td>
<td>55 (60.4%)</td>
</tr>
<tr>
<td>Total duration of follow-up, months*</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>70 (41.3)</td>
</tr>
</tbody>
</table>

*SD = standard deviation
* A patient may have multiple sites of distant metastasis
* Length of follow-up was the duration of time between the date of locally advanced or metastatic GEP-NET diagnosis and death or end of patient record


This study was sponsored by Ipsen.
The sequencing of lanreotide (LAN) after octreotide LAR (OCT) for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

Wasif M. Saif,1 Rohan Parikh,1 David Ray,1 James A. Kaye,1 Samantha K. Kurosky,1 Katharine Thomas,1 Robert A. Ramirez,2 Thorvardur Halldarason,2 Thomas J.R. Beveridge,3 Beloo Mirakhor,1 Catherine A. Lubeck,1 Saurabh Nagar,2 Heliosa Soares3

1Tufts University School of Medicine, Boston, MA, USA; 2RTI Health Solutions, Research Triangle Park, NC, USA; 3Ipsen Biopharmaceuticals, Boston, MA, USA; 4RTI Health Solutions, Winston-Salem, MA, USA

Treatment with long-acting octreotide and reason(s) for transition
• After initial GEP-NET diagnosis, patients began treatment with long-acting octreotide after a median (IQR) of 17.0 (24.7) months and took long-acting octreotide for a mean (SD) of 38.4 (32.8) months.
• The most common known reasons for transition were progressive disease (n=20, 22.0%), formulary change (n=14, 15.4%), and patient preference (n=9, 9.9%). The reason for transition was not documented for more than one-third of patients (n=33, 35.3%).
• At the time of their transition to lanreotide, more than half of patients (n=52, 57.1%) had nonprogressive disease, 28 (30.8%) patients had clinically defined progressive disease (9.8%) patients assessed based on imaging), and the remainder had unknown disease status.

Treatment with lanreotide and tumor assessment
• At the end of study follow-up, 67 (73.6%) patients were still receiving lanreotide treatment, and the Kaplan-Meier estimated median (95% confidence interval (CI)) duration was 24.7 (10.5-59.6) months.
• Clinician-defined progressive disease was observed for 22 (24.2%) patients after initiating lanreotide monotherapy (20 of 22 [90.9%] patients were assessed based on imaging) (Figure 2).
• The median (95% CI) clinical PFS after treatment with lanreotide was estimated to be 23.7 months (20.2, not estimable) (Figure 3a).
• Among patients with progressive disease at the time of transition to lanreotide in > 281, 13 (46.4%) experienced subsequent clinician-defined disease progression while receiving lanreotide monotherapy (13 of 13 [100%] patients were assessed based on imaging) (Figure 2).
• Among patients who had progressive disease at the time of transition to lanreotide, the median (95% CI) clinical PFS was estimated to be 15.3 months (11.4, not estimable) (Figure 3b).
The sequencing of lanreotide (LAN) after octreotide LAR (OCT) for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

Wasil M. Saif,1 Rohan Parikh,1 David Ray,2 James A. Kaye,3 Samantha K. Kurosky,1 Katharine Thomas,1 Robert A. Ramirez,2 Thorvardur Halfdanarson,8 Thomas J.R. Beveridge,3 Beloo Mirakhur,2 Catherine A. Lubeck,2 Saurabh Nagar,2 Heliosa Soares2

1Tufts University School of Medicine, Boston, MA, USA; 2RTI Health Solutions, Research Triangle Park, NC, USA; 3Ipsen Biopharmaceuticals, Boston, MA, USA; 4RTI Health Solutions, Wattham, MA, USA; 5Oncology Medical Center-Keller, Neuroendocrine Tumor Program, Keller, TX, USA; 6Mayo Clinic, Rochester, MN, USA; 7University of New Mexico Medical School, Albuquerque, NM, USA.

LIMITATIONS

• Patients included in the study were selected by convenience sample, so study findings may not be generalizable to the overall population of patients with locally advanced or metastatic GEP-NET.

• The type and frequency of testing to assess tumor status in a real-world practice may differ (and is typically more variable) from those required in a clinical trial protocol. Therefore, PFS estimates from this study should be compared with clinical trial estimates with these limitations in mind.

• Evaluation of progression in this study was not restricted to tumor imaging only and assessment through symptoms, biochemical tests, and/or clinical judgement was allowed. However, more than 90% of patients were determined to have progressive disease using tumor imaging.

• The requirement for 90 days of lanreotide treatment after transition could have introduced immortal time bias into survival estimates.

CONCLUSION

• This retrospective medical record review assessed the feasibility of sequencing from long-acting octreotide monotherapy to lanreotide monotherapy among patients with locally advanced GEP-NET across multiple sites in the US.

• After receiving long-acting octreotide for an average of 38 months, the median clinical PFS for lanreotide monotherapy was estimated to be 23.7 months (95% CI, 20.2 to not estimable).

• Our study suggests that patients with locally advanced or metastatic GEP-NETs previously treated with long-acting octreotide monotherapy can be safely transitioned to lanreotide monotherapy.

- The clinical PFS observed among patients who had either nonprogressive or progressive disease at the time of transition from long-acting octreotide to lanreotide reinforces the possibility of sequencing lanreotide after long-acting octreotide.

References


CONTACT INFORMATION

David Ray, PharmD, MBA
Ipsen Biopharmaceuticals, Inc.
205-Allen Road, 3rd Floor
Bedford Ridge, NJ 07623 USA
E-mail: davidray@ipsen.com
Dr. Barrios was unable to review the abstract, but meets all ICMJE authorship criteria to qualify as an author of this poster.

This study was sponsored by Ipsen